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C12N 15/12, 5/10, C07K 14/47, C12Q 1/68, A61K 38/17

A3

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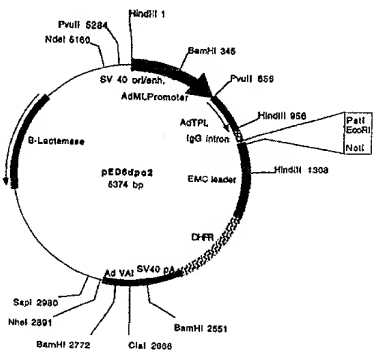
30 July 1998 (30.07.98)

(54) Title: SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

(57) Abstract

Novel proteins are disclosed.



Plasmid name: pED6dpc2
Plasmid size: 5374 bp

Comments/References: pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SST cDNAs are cloned between EcoRI and NotI. pED vectors are described in Kaufman et al.(1991), NAR 19: 4485-4490.

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EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

Intern[illegible]al Application No
PCT/US 97/19857

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C12N5/10 C07K14/47 C12Q1/68 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	T. FUJIWARA ET AL.: "Human fetal brain cDNA 5'end GEN-430B12" EMBL SEQUENCE DATABASE, 31 August 1995, HEIDELBERG, FRG, XP002054811 Accession no. D56480 ---	1-8
A	L. HILLIER ET AL.: "yz37e06.s1 Homo sapiens cDNA clone 285250 3'" EMBL SEQUENCE DATABASE, 15 March 1996, HEIDELBERG, FRG, XP002054812 Accession no. N66290 --- -/--	1-8

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
6 February 1998	27 -05- 1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	HORNIG H.

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	L. HILLIER ET AL.: "zd40d05.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343113 5'" EMBL SEQUENCE DATABASE, 16 June 1996, HEIDELBERG, FRG, XP002054813 Accession no. W67393 ---	1-8
A	L. HILLIER ET AL.: "zd40d05.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343113 3'" EMBL SEQUENCE DATABASE, 16 June 1996, HEIDELBERG, FRG, XP002054814 Accession no. W67150 ---	1-8
A	ADAMS M D ET AL: "3,400 NEW EXPRESSED SEQUENCE TAGS IDENTIFY DIVERSITY OF TRANSCRIPTS IN HUMAN BRAIN" NATURE GENETICS, vol. 4, no. 3, pages 256-267, XP000611495 see the whole document ---	1-8
A	JACOBS K ET AL: "A novel method for isolating eukaryotic cDNA clones encoding secreted proteins." KEYSTONE SYMPOSIUM ON DENDRITIC CELLS: ANTIGEN PRESENTING CELLS OF T AND B LYMPHOCYTES, TAOS, NEW MEXICO, USA, MARCH 10-16, 1995. JOURNAL OF CELLULAR BIOCHEMISTRY SUPPLEMENT 0 (21A). 1995. 19. ISSN: 0733-1959, XP002027246 abstract no. C1-207 see abstract ---	1-8
A	EP 0 510 691 A (OSAKA BIOSCIENCE INST) 28 October 1992 see the whole document ---	1-8
A	WO 94 07916 A (MERCK & CO INC ;SCHMIDT AZRIEL (US); RODAN GIDEON A (US); RUTLEDGE) 14 April 1994 see the whole document ---	1-8
A	WO 90 05780 A (OREGON STATE) 31 May 1990 see the whole document ---	1-8
A	WO 90 14432 A (GENETICS INST) 29 November 1990 see the whole document ---	1-8
A	WO 96 17925 A (IMMUNEX CORP) 13 June 1996 see the whole document ---	1-8

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern ial Application No
PCT/US 97/19857

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	R.J. KAUFMAN ET AL.: "Effect of von Willebrand factor coexpression on the synthesis and secretion of factor VIII in chinese hamster ovary cells" MOL. CELL. BIOL., vol. 9, no. 3, March 1989, ASM WASHINGTON, DC,US, pages 1233-1242, XP002041592 see the whole document	1-8
A	R.J. KAUFMAN ET AL.: "The phosphorylation state of eucaryotic initiation factor 2 alters translation efficiency of specific mRNAs" MOL. CELL. BIOL., vol. 9, no. 3, March 1989, ASM WASHINGTON, DC,US, pages 946-958, XP002041593 see the whole document	1-8
A	R.J. KAUFMAN ET AL.: "Improved vectors for stable expression of foreign genes in mammalian cells by use of the untranslated leader sequence from EMC virus" NUCLEIC ACIDS RESEARCH, vol. 19, no. 16, 1991, IRL PRESS LIMITED,OXFORD,ENGLAND, pages 4485-4490, XP002041594 cited in the application see the whole document	1-8
A	US 5 536 637 A (JACOBS KENNETH) 16 July 1996 cited in the application see the whole document	1-8
P,A	WO 97 07198 A (GENETICS INSTITUT) 27 February 1997 see the whole document	1-8
P,A	WO 97 25427 A (GENETICS INST) 17 July 1997 see the whole document	1-8

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

...formation on patent family members

International Application No
PCT/US 97/19857

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0510691 A	28-10-92	CA 2067031 A	27-10-92
		JP 5184368 A	27-07-93
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		DE 68928137 T	19-02-98
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		EP 0839196 A	06-05-98
		WO 9704097 A	06-02-97
WO 9725427 A	17-07-97	AU 1532697 A	01-08-97

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/ 19857

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
See Annex

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See annex

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-8

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-8

A composition comprising an isolated protein encoded by a polynucleotide sequence of SEQ ID no.25; said composition further comprising a pharmaceutical acceptable carrier; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said composition; a composition comprising a protein, wherein said protein comprises an aminoacid sequence of SEQ ID no.26; said composition comprising a pharmaceutical acceptable carrier; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said composition;

2. Claims: 9-10

A composition comprising an isolated protein encoded by a polynucleotide sequence selected from the group of SEQ ID no.4; a composition comprises a protein, wherein said protein comprises an amino acid sequence selected from the group of SEQ ID no.5;

3. Claims: 11-12

Idem as subject 2 but limited to SEQ ID nos. 7 and 8.

4. Claims: 13-14

Idem as subject 2 but limited to SEQ ID nos. 10 and 11.

5. Claims: 15-16

Idem as subject 2 but limited to SEQ ID nos. 13 and 14.

6. Claims: 17-18

Idem as subject 2 but limited to SEQ ID nos. 16 and 17.

7. Claims: 19-20

Idem as subject 2 but limited to SEQ ID nos. 19 and 20.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. Claims: 21-22

Idem as subject 2 but limited to SEQ ID nos. 22 and 23.

Remark : Although claims 3,8 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein

of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 µg to about 100 mg (preferably about 0.1ng to about 10 mg, more preferably about 0.1 µg to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal and monoclonal antibodies which specifically react with the protein. Such

antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J. Amer.Chem.Soc. 85, 2149-2154 (1963); J.L. Krstenansky, *et al.*, FEBS Lett. 211, 10 (1987). Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where abnormal expression of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and

polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorbtion of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

Patent and literature references cited herein are incorporated by reference as if fully set forth.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Jacobs, Kenneth
McCoy, John
LaVallie, Edward
Racie, Lisa
Merberg, David
Treacy, Maurice
Spaulding, Vikki
Agostino, Michael J.

(ii) TITLE OF INVENTION: SECRETED PROTEINS

(iii) NUMBER OF SEQUENCES: 26

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Genetics Institute, Inc.
(B) STREET: 87 CambridgePark Drive
(C) CITY: Cambridge
(D) STATE: Massachusetts
(E) COUNTRY: U.S.A.
(F) ZIP: 02140

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Sprunger, Suzanne A.
(B) REGISTRATION NUMBER: 41,323

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (617) 498-8284
(B) TELEFAX: (617) 876-5851

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 322 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CAAGAAGGAC GAGCCCAAGA GCAGCGAGGA GGCGCTCATC GTCCCTCCGG ATGCCGTGGC 60

GGTGGATTGC AAGGACCCGG GTGACGTGGT TCCGGTTGGA CAGAGGAGAG CGTGGTGTTG 120

GTGCATGTGT TTCGGACTGG CCTTCATGCT TGCTGGCGTC ATCCTCGGAG GGGCGTACCT 180

GTACAAGTAT TTTGCTCTTC AGCCAGATGA TGTGTACTAC TGTGGACTAA AGTACATCAA 240

AGATGACGTC ATCCTGAACG AGCCTTCTGC GGATGCCCCA GCTGCTCGCT ACCAGACAAT 300

TGAAGAGAAC ATTAAGATCT TT 322

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 66 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Cys Phe Gly Leu Ala Phe Met Leu Ala Gly Val Ile Leu Gly Gly
1 5 10 15

Ala Tyr Leu Tyr Lys Tyr Phe Ala Leu Gln Pro Asp Asp Val Tyr Tyr
20 25 30

Cys Gly Leu Lys Tyr Ile Lys Asp Asp Val Ile Leu Asn Glu Pro Ser
35 40 45

Ala Asp Ala Pro Ala Ala Arg Tyr Gln Thr Ile Glu Glu Asn Ile Lys
50 55 60

Ile Phe
65

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 145 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CCCCACCCTT NACATTTTGT GCAGTGATTA TTNTTTAAAN TNTTNTTTCA TGTAAGTAGC 60

AAACAGGGCT TTACTATNTT TTCATCTCAT TAATTCAATT AAAACCATTA CCTTAAAAAA 120

AAAAAANAAA AAAAAAAAA AAAAA 145

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 268 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

GTTTGACCTG GCTGGAATAA CGTGTGGGCA CTTCCTTGAA CCTTTCTGGA CCTTCTTTGG 60

TGCAACCCTG ATTGGGAAAG CAATCATTAA AATGCATATC CAGAAAATAT TTGTTATAGT 120

AACTTTCAGC AAGCACATCG TGGAGCAGAT GGTGACTTTC ATTGGTGCTG TCCCCGGCAT 180

AGGTCCGTCT CTGCAGAAGC CTTTTCAAGA GTACCTGGAG GCGCAGCGGC AGAAGCTTCA 240

TCACAGAAGT GAAGCGGGCA CACCGCAG 268

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Met His Ile Gln Lys Ile Phe Val Ile Val Thr Phe Ser Lys His Ile
1 5 10 15

Val Glu Gln Met Val Thr Phe Ile Gly Ala Val Pro Gly Ile Gly Pro
20 25 30

Ser Leu Gln Lys Pro Phe Gln Glu Tyr Leu Glu Ala Gln Arg Gln Lys
35 40 45

Leu His His Arg Ser Glu Ala Gly Thr Pro Gln
50 55

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 138 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GAGACAGTAT AAGGAAAATC TGGTTGGTGT CTNACAAGTG AGCNGACACC ATTTTTTATT 60

CTGTGTATTT AGAATGAAGT CTTGAAAAAA ACTTAAAAAA GACAACTTTA ATCATTCCAA 120

AAAAAAAAAA AAAAAAAA 138

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 415 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

AACAGAGAAA GAAACCACCC AAGAGTATAT CAGAATCGGG ATTTCCGAGG TCACAACAGA 60

GGCTATAGAA GGCCCTATTA TTTCCGTGGG CGTAACAGAG GCTTTTATCC ATGGGGCCAA 120

TATAACCGAG GAGGCTATGG AAACTACCGC TCAAATTGGC AGAATTACCG GCAAGCATAC 180

AGTCCTCGTC GAGGCCGTTC AAGATCCCGG NCCCCAAAAA AAAGNTCCCC TCCNCCANGG 240

TCNAGAACCC NTCCNAAAAC CNCTAATANT TCTNCTCCTA ACCGNTCANG GCCCCCCNCN 300

CCCCCCCTTC CTCCCCCCAN CCNTACCCAA TTTAATNCTC CTAACCCCAN TTNTNCAAAG 360

AAAAAAAATT CCCCTCCNAA GNATACCCGG CCNNCTCAGG CTNCNGGGAA TANCC 415

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 92 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Glu Thr Thr Ala Gln Ile Gly Arg Ile Thr Gly Lys His Thr Val
1 5 10 15

Leu Val Glu Ala Val Gln Asp Pro Gly Pro Gln Lys Lys Xaa Pro Leu
20 25 30

Xaa Xaa Gly Xaa Glu Pro Xaa Xaa Lys Pro Leu Ile Xaa Leu Leu Leu
35 40 45

Thr Xaa Xaa Gly Pro Pro Xaa Pro Pro Phe Leu Pro Pro Xaa Xaa Pro
50 55 60

Asn Leu Xaa Leu Leu Thr Pro Xaa Xaa Gln Arg Lys Lys Ile Pro Leu
65 70 75 80

Xaa Xaa Ile Pro Gly Xaa Leu Arg Leu Xaa Gly Ile
85 90

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 268 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

AATTTGCCGA GTGGTGCCGG GTATCAGTTT GGGAAANACC AAGGTCAGTT TGACCATGGT 60

TTTGGGTCCC NGNGTCCATC CAAAAAGNGC CCTGTGGGNA AGNGTNCACC ATCCAATGGG 120

TNCAAANATG GNTNATTTCA GNAGGNGGAG NGTGCTGNTT CAGGNGGNGC AGCCTATANA 180

AAGNGGTATT TAGNAGAGCA GAAGACAGAG GATGGGAAAG ATNAGGGACA GNAACAAACN 240

AATACCGNTN AAAAAAAAAA AAAAAAAA 268

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 323 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

ACAGAGCCTC TACCTGGCAG GAAACAAGTC CGGGATACTT TGGCAGCAAT CTCAGAAGTT 60

CTTTATGTTG ATTTGCTAGA AGGGGATACA GAATGCCATG CTAGATTTAA AACTCCTGAG 120

GATGCTCAAG CAGTAATAAA TGCCTATACA GAAATTAACA AGAAACACTG CTGGAAACTC 180

GAGATCCTTT CTGGTGATCA CGAACAAAGG TATTGGCAGA AGATTTTGGT TGATAGAAAG 240

GCAANNNTTA ATCAGCCTCG GGAAAAGAAA AGAGNGGTGA AAAGTTAATC ACCAGAGCTG 300

AAAAGATTAG ACTGGCAAAG ACT 323

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 95 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Thr Glu Pro Leu Pro Gly Arg Lys Gln Val Arg Asp Thr Leu Ala Ala
1 5 10 15

Ile Ser Glu Val Leu Tyr Val Asp Leu Leu Glu Gly Asp Thr Glu Cys
20 25 30

His Ala Arg Phe Lys Thr Pro Glu Asp Ala Gln Ala Val Ile Asn Ala

35 40 45

Tyr Thr Glu Ile Asn Lys Lys His Cys Trp Lys Leu Glu Ile Leu Ser
50 55 60

Gly Asp His Glu Gln Arg Tyr Trp Gln Lys Ile Leu Val Asp Arg Lys
65 70 75 80

Ala Xaa Xaa Asn Gln Pro Arg Glu Lys Lys Arg Xaa Val Lys Ser
85 90 95

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 190 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

TTTTTAATTA AAAGNAANAT TTTTGTTCCT NAAATTGTAN ATAAGAATTT TTTTTAGNGA 60

CNAANATGAN GNANACCACN ATTTTTTTTA AANATTTTAT TTGTTGAAAT TATTTTAGAN 120

GTCNGTGTCA GGNGATTTAG TAAATAAANG TGTTTTGGAC NTTTAAAAAA AAAAAAAAAA 180

AAAAAAAAAA 190

(2) INFORMATION FOR SEQ ID NO:13:

(i) *SEQUENCE CHARACTERISTICS:*
(A) LENGTH: 294 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

GGCATCTGCA ACCTGCTCCT TTACTTCGCC TTCTACATCA TCATGAAGCT CCGGAGTGGG 60

GAGAGGATCA AGCTCATCCC CCTGCTCTGC ATCGTTTGCA CCTCCGTGGT CTGGGGCTTC 120

GCGCTCTTCT TCTTCTTCCA GGGACTCAGC ACCTGGCAGA AAACCCCTGC AGAGTCGAGG 180

GAGCACAACC GGGACTGCAT CCTCCTCGAC TTCTTTGACG ACCACGACAT CTGGCACTTC 240

CTCTCCTCCA TCGCCATGTT TCGGGTCCTT CCTGGTGTTT GCTGACACTG GATG 294

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 80 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Met Lys Leu Arg Ser Gly Glu Arg Ile Lys Leu Ile Pro Leu Leu Cys
1 5 10 15

Ile Val Cys Thr Ser Val Val Trp Gly Phe Ala Leu Phe Phe Phe Phe
20 25 30

Gln Gly Leu Ser Thr Trp Gln Lys Thr Pro Ala Glu Ser Arg Glu His
35 40 45

Asn Arg Asp Cys Ile Leu Leu Asp Phe Phe Asp Asp His Asp Ile Trp
50 55 60

His Phe Leu Ser Ser Ile Ala Met Phe Arg Val Leu Pro Gly Val Cys
65 70 75 80

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 230 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ACCCCAGATG CTGAGGATGG GGGAGCTCAG GCGGGGCNTC TGCTTNGGGG ATGGGAATGT 60

GTTTTTCTCC CAAACTTGTT TTTATAGCTC TGCTTGAAGG GCTGGGAGAT GAGGTGGGTC 120

TGGATCTTTT CTCAGAGCGT CTCCATGCTA TGGTTGCATT TCCGTTTTCT ATGAATGAAT 180

TTGCATTCAA TAAACAACCA GACTCAAAAA AAAAAAAAAA AAAAAAAAAA 230

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 495 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

GACCTGCCTT CCTGCTCTTC TAGGTAGTCA CACTTCACTA AAGTGTCATC CACCAGTGTG 60

TTGAATCCGA AGAATGACAA TTTTCTACCA CTGGTGTAAA AAACAAACAT TTGAAGACCC 120

TTGTGCATTG TGTGTCACAA AGCTAAATAC ATGGAAATCG TTAATATCGC TGATATTAAG 180

TAATTTCCCC ACTCTGAGTG AATACTTTGA TGATTGCCAA CAGTGGCTAA TAAAATGACG 240

GCTACCACAC TCATGGGTCA CTGGGGCTGC GCAGGGCTCT TTGAGGTGGG TGGCTTCTTT 300

TGGAAAGTAC TATGAACGTC TCGAAGCAGT ATTCTAGTGA TAAGAATTCT TAACATAGCC 360

AAGCGCCCCA CGTTTGTTCC CCACGTTTGT TCCCCTTTTC TGTTTGAAAA ACCTGTTCTG 420

GTAGCTCCNC AAGAGAGATG ATACTGACTT TTTAAATTTT TTACAANAGT CTGTATTCCT 480

GATATGCCTA TATTT 495

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Thr Ser Arg Ser Ser Ile Leu Val Ile Arg Ile Leu Asn Ile Ala Lys
1 5 10 15

Arg Pro Thr Phe Val Pro His Val Cys Ser Pro Phe Leu Phe Glu Lys
20 25 30

Pro Val Leu Val Ala Pro Gln Glu Arg
35 40

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

GAAAAAAAAA AAAAAAAA 18

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 285 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

CACGAAGGGT TTCAAGGTCT GTCTTAGTTC TCATTCTCAA GATTGTTTCC AGTTGCAAGT 60

TAGAGGCAAG CCAGCTAGCT GCCCAGCCTT AACTCTGTTC AGTGCCCTGT TACTAACATT 120

TTTTAACAGA TTGGNTTCTA CATGTTTAAA GTATCCAGCG TTGGATTTTA CCTCTTGCTA 180

GTTCCATTTG TCCCTGGTGC TGCTTTTAAA GGTATAGGGC CCTGTGAAGT GGANTATGTA 240

CGCAGTTGGC CTGGTGATGT ATCTGTGCCT GTTTTATCTT CTCCC 285

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 48 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met Phe Lys Val Ser Ser Val Gly Phe Tyr Leu Leu Leu Val Pro Phe
1 5 10 15

Val Pro Gly Ala Ala Phe Lys Gly Ile Gly Pro Cys Glu Val Xaa Tyr
20 25 30

Val Arg Ser Trp Pro Gly Asp Val Ser Val Pro Val Leu Ser Ser Pro
35 40 45

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 350 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

TTCCNTATGT AAGATGTCAT ACTGCAGATT TAAAATATAG ACTATCAATA AAATGCATGA 60

AGTGATCATT TGTGCTTGAT CATCTCTCCT TGGGTTTTTC TTTAAAAAGG GGAATCTGCT 120

ATAAAGGTTC TGTTGCTTCA AACCAATGTC AAATAGACTT GATTTTTAGA GTCATGGAAT 180

TACAGTGCAA CCTTGATTTT TATTCCCCTC ACTGNTATGA GTGTGGGCAG GTACTGGTTT 240

ATATGTTATA ACTTCCGTTT TATCTGTGTT GTGTAGTTGA ATGGCTTAAT CGTTGAGTGG 300

TAAAATAAAA GATTATATTC CAATACAAGG AAAAAAAAAA AAAAAAAAAA 350

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 517 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CACGAGGCCT CGTGCCAACA GGAAAGTTGC TTTGTTTTGC TTCGAGATGG CTGCGGGGAT 60

GTNTTTGGAA CATTATCTGG ACAGTATTGA AAACCTCCCG TTTGAATTAC AGAGAAACTT 120

TCAGCTCATG AGGGACCTAG ACCAAAGGAC AGAGGACCTG AAGGCTGAAA TTGACAAGTT 180

GGCCACTGAA TATATGAGTA GCGCCCGCAG CCTGAGCTCC GAGGAGAAGC TGGCCCTTCT 240

CAGACAGATC CAGGAGGCCT ATGGCAAGTG CAAGGAATTT GGTGACGACA AGGTGCAGCT 300

GGCCATGCAG ACCTATGAGA TGGTAGACAA ACACATTCGG CGGCTGGACA CAGACCTGGC 360

CCGTTTTGAG GCTGATCTGA AGGAGAAACA GATCGAGTCC AGTGACTATG ACAGCTCTTC 420

TAGCAAAGGC AAAAAGAGCC GGACCCAAAA GGAGAAAAAA GCTGCCAGAG CCCGTTCCAA 480

AGGGAAAAAC TCAGATGAAG AAGCCCCCAA GGCTGCC 517

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 157 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Met Ala Ala Gly Met Xaa Leu Glu His Tyr Leu Asp Ser Ile Glu Asn
1 5 10 15

Leu Pro Phe Glu Leu Gln Arg Asn Phe Gln Leu Met Arg Asp Leu Asp
20 25 30

Gln Arg Thr Glu Asp Leu Lys Ala Glu Ile Asp Lys Leu Ala Thr Glu
35 40 45

Tyr Met Ser Ser Ala Arg Ser Leu Ser Ser Glu Glu Lys Leu Ala Leu
50 55 60

Leu Arg Gln Ile Gln Glu Ala Tyr Gly Lys Cys Lys Glu Phe Gly Asp
65 70 75 80

Asp Lys Val Gln Leu Ala Met Gln Thr Tyr Glu Met Val Asp Lys His
85 90 95

Ile Arg Arg Leu Asp Thr Asp Leu Ala Arg Phe Glu Ala Asp Leu Lys
100 105 110

Glu Lys Gln Ile Glu Ser Ser Asp Tyr Asp Ser Ser Ser Ser Lys Gly

115 120 125

Lys Lys Ser Arg Thr Gln Lys Glu Lys Lys Ala Ala Arg Ala Arg Ser
130 135 140

Lys Gly Lys Asn Ser Asp Glu Glu Ala Pro Lys Ala Ala
145 150 155

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 246 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

TCCTGTGGTG AGGGCTAGGT GTGNTCNNCN CTNTTATTCT CCATTCCCTT CCTGCTTTTT 60

TCATGGTGGG GGATCCACCA GGTCATNTAG GCTCTGGCCC TAGTTGAAGG GGCACCCCTT 120

CNTCTGTGCC AAGAGGATTC ATCCTGGGAG AGGGGGCAAG GTGGAATGCA GATAACTCAC 180

ATGTAAAAGG AACTTGGGTA GGTAAATAAA AGCTATACAT GTTGAAAAAA AAAAAAAAAA 240

AAAAAA 246

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 896 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

CACGAGGCGG TGGACTGCAA GGACCCAGAT GATGTGGTAC CAGTTGGCCA AAGAAGAGCC 60

TGGTGTTGGT GCATGTGCTT TGGACTAGCA TTTATGCTTG CAGGTGTTAT TCTAGGAGGA 120

GCATACTTGT ACAAATATTT TGCACTTCAA CCAGATGACG TGTACTACTG TGGAATAAAG 180

TACATCAAAG ATGATGTCAT CTTAAATGAG CCCTCTGCAG ATGCCCCAGC TGCTCTCTAC 240

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Leu Thr Ala Tyr Leu Asp Leu Asn Leu Asp Lys Cys Tyr Val Ile Pro
            100                 105                 110

Leu Asn Thr Ser Ile Val Met Pro Pro Arg Asn Leu Leu Glu Leu Leu
        115                 120                 125

Ile Asn Ile Lys Ala Gly Thr Tyr Leu Pro Gln Ser Tyr Leu Ile His
    130                 135                 140

Glu His Met Val Ile Thr Asp Arg Ile Glu Asn Ile Asp His Leu Gly
145                 150                 155                 160

Phe Phe Ile Tyr Arg Leu Cys His Asp Lys Glu Thr Tyr Lys Leu Gln
                165                 170                 175

Arg Arg Glu Thr Ile Lys Gly Ile Gln Lys Arg Glu Ala Ser Asn Cys
            180                 185                 190

Phe Ala Ile Arg His Phe Glu Asn Lys Phe Ala Val Glu Thr Leu Ile
        195                 200                 205

Cys Ser
    210
```

What is claimed is:

1. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25 from nucleotide 73 to nucleotide 702;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25 from nucleotide 118 to nucleotide 702;

(d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AE648_1i deposited under accession number ATCC 98237;

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AE648_1i deposited under accession number ATCC 98237;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AE648_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AE648_1i deposited under accession number ATCC 98237;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:26;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

2. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

3. A method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition of claim 2.

4. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:26;

(b) the amino acid sequence of SEQ ID NO:26 from amino acid 1 to amino acid 34;

(c) fragments of the amino acid sequence of SEQ ID NO:26; and

(d) the amino acid sequence encoded by the cDNA insert of clone AE648_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

5. The composition of claim 4, wherein said protein comprises the amino acid sequence of SEQ ID NO:26.

6. The composition of claim 4, wherein said protein comprises the amino acid sequence of SEQ ID NO:26 from amino acid 1 to amino acid 34.

7. The composition of claim 4, further comprising a pharmaceutically acceptable carrier.

8. A method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition of claim 7.

9. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4 from nucleotide 92 to nucleotide 268;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AE693_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AE693_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AE693_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AE693_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:5;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:5 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

10. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:5;

(b) fragments of the amino acid sequence of SEQ ID NO:5; and

(c) the amino acid sequence encoded by the cDNA insert of clone AE693_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

11. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 137 to nucleotide 412;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK438_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK438_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK438_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK438_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:8;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

12. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:8;

(b) fragments of the amino acid sequence of SEQ ID NO:8; and

(c) the amino acid sequence encoded by the cDNA insert of clone AK438_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

13. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:10;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:10 from nucleotide to nucleotide 285;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK609_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK609_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK609_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK609_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:11;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:11 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

14. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:11;

(b) fragments of the amino acid sequence of SEQ ID NO:11; and

(c) the amino acid sequence encoded by the cDNA insert of clone AK609_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

15. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 43 to nucleotide 282;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 118 to nucleotide 282;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM1060_1i deposited under accession number ATCC 98237;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM1060_1i deposited under accession number ATCC 98237;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM1060_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM1060_1i deposited under accession number ATCC 98237;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:14;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

16. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:14;

(b) fragments of the amino acid sequence of SEQ ID NO:14; and

(c) the amino acid sequence encoded by the cDNA insert of clone AM1060_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

17. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:16;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:16 from nucleotide 316 to nucleotide 438;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AQ2_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AQ2_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AQ2_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AQ2_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:17;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:17 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

18. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:17;

(b) the amino acid sequence of SEQ ID NO:17 from amino acid 1 to amino acid 25;

(c) fragments of the amino acid sequence of SEQ ID NO:17; and

(d) the amino acid sequence encoded by the cDNA insert of clone AQ2_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

19. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 142 to nucleotide 285;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone K433_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone K433_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone K433_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone K433_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:20;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

20. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:20;

(b) the amino acid sequence of SEQ ID NO:20 from amino acid 1 to amino acid 30;

(c) fragments of the amino acid sequence of SEQ ID NO:20; and

(d) the amino acid sequence encoded by the cDNA insert of clone K433_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

21. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:22;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:22 from nucleotide 47 to nucleotide 517;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone L256_1i deposited under accession number ATCC 98237;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone L256_1i deposited under accession number ATCC 98237;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone L256_1i deposited under accession number ATCC 98237;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone L256_1i deposited under accession number ATCC 98237;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:23;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:23 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

22. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:23;

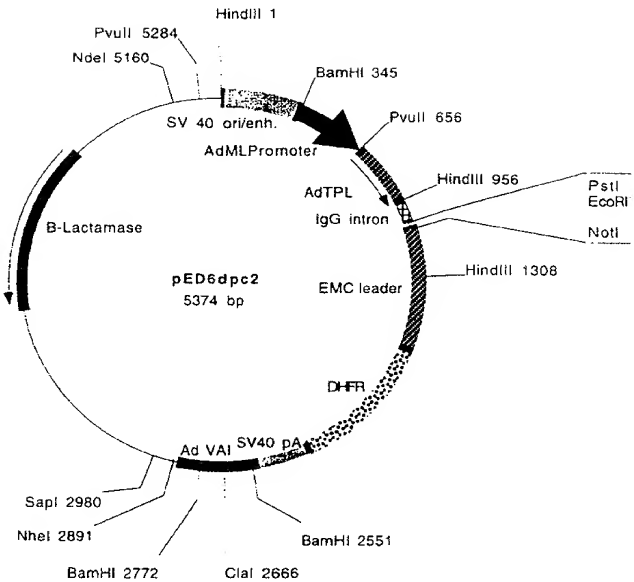
(b) the amino acid sequence of SEQ ID NO:23 from amino acid 8 to amino acid 157;

(c) fragments of the amino acid sequence of SEQ ID NO:23; and

(d) the amino acid sequence encoded by the cDNA insert of clone L256_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins.

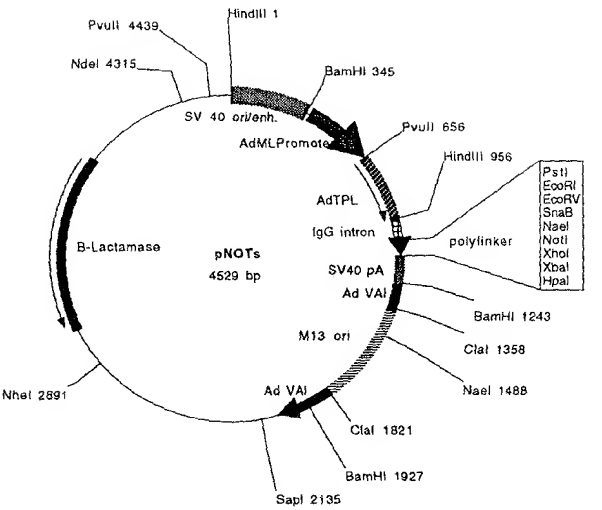
FIGURE 1A



Plasmid name: pED6dpc2
Plasmid size: 5374 bp

Comments/References: pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SST cDNAs are cloned between EcoRI and NotI. pED vectors are described in Kaufman et al.(1991). NAR 19: 4485-4490.

FIGURE 1B



Plasmid name: pNOTs
Plasmid size: 4529 bp

Comments/References: pNOTs is a derivative of pMT2 (Kaufman et al,1989. Mol.Cell.Biol.9:1741-1750). DHFR was deleted and a new polylinker was inserted between EcoRI and HpaI. M13 origin of replication was inserted in the ClaI site. SST cDNAs are cloned between EcoRI and NotI